



Sociodemographic Factors Associated with HAART Non-adherence Among HIV-Infected Adults in Lerato Clinic, Bertha Qxowa Hospital, Gauteng, South Africa

Nzale Nzali Ntumbanzondo Arnold^{1,2}, Nzale Nzali Kadiombo Tshilela Anastasie³, Longo-Mbenza Benjamin^{1,2,3,4,*}, Nge Okwe Augustin¹, Kisoka Lusunsi Christian¹, Kamangu Ntambwe Eric⁵, Ngonde Mambakasa Ange Christian⁶

¹Department of Public Health, Lomo University of Research, Kinshasa, Democratic Republic of Congo

²Faculty of Medicine, Joseph Kasa-Vubu University, Boma, Democratic Republic of Congo

³Department of Internal Medicine, University of Kinshasa, Kinshasa, Democratic Republic of Congo

⁴Faculty of Health Sciences, Walter Sisulu University, Mthatha, South Africa

⁵Department of Basic Sciences, University of Kinshasa, Kinshasa, Democratic Republic of Congo

⁶Department of Family Medicine, Congo Protestant University, Kinshasa, Democratic Republic of Congo

Email address:

longombenza@gmail.com (Longo-Mbenza B.), longo.mbenza@unikin.ac.cd (Longo-Mbenza B.)

*Corresponding author

To cite this article:

Nzale Nzali Ntumbanzondo Arnold, Nzale Nzali Kadiombo Tshilela Anastasie, Longo-Mbenza Benjamin, Nge Okwe Augustin, Kisoka Lusunsi Christian, Kamangu Ntambwe Eric, Ngonde Mambakasa Ange Christian. Sociodemographic Factors Associated with HAART Non-adherence Among HIV-Infected Adults in Lerato Clinic, Bertha Qxowa Hospital, Gauteng, South Africa. *International Journal of HIV/AIDS Prevention, Education and Behavioural Science*. Vol. 8, No. 1, 2022, pp. 30-35. doi: 10.11648/j.ijhpebs.20220801.16

Received: April 28, 2022; Accepted: May 17, 2022; Published: May 26, 2022

Abstract: *Background and aims:* HIV/AIDS is a pandemic infection with socio-economic factors associated with HAART non-adherence. It is well established that the clinical efficiency of HAART in suppressing the HIV virus toward a long survival needs a non-adherence rate of less than 5%. South Africa is facing a high level of HIV/AIDS rate, where a low level of non-adherence is needed. *Methods:* The investigator conducted a cross-sectional study at Lerato Clinic in Germiston, Gauteng, South Africa from September 2019 to December 2019. Non-adherence was measured by doing first a pill count for all eligible patients every working day preceding inclusion by self-reported method following quantitative (missing dosage of ART). Non-adherence was defined as taking their medication $\leq 95\%$ of the time. A threshold of non-adherence $> 5\%$ was considered high, with $P < 0.05$ statistically significant. *Results:* Out of 278 patients (56%, $n = 156$ Males; 44%, $n = 122$ Females) with a sex ratio of 1.3 Male \div 1 Female, all were evaluated. The majority of patients were younger than 45 years (67%, $n = 187$), single (43%, $n = 120$), Blacks (75.8%, $n = 211$), those with High School level (48%, $n = 134$), and Jobless people (45%, $n = 126$). Out of all patients, 19% ($n = 52$) were recognized as non-adherents to HAART in Lerato clinic in Betha Qxowa Hospital, Germiston, Gauteng, South Africa. However, there was no significant univariate association ($P = 0.452$) between Ethnic groups and non-adherence to HAART: 19.4% ($n = 41/211$) among blacks, 13.9% ($n = 5/36$) among Caucasians/ Whites, 7.7% ($n = 1/13$) among coloured, and 27.8% ($n = 5/18$) among Indians. The univariate risk of non-adherence to HAART was respectively multiplied by 2, 3, 5, and 4 by male gender, aging, low education level, and Widowed. *Conclusion:* Our study found the level of non-adherence to be 19%, very high, but comparable to other developing countries. Stigma or fear of disclosure, being away from home, too busy with other things, the side-effects, and toxicity of ART drugs, are the main obstacles to ART adherence.

Keywords: Sociodemographic Factors Associated, Non-adherence to HAART, HIV/AIDS

1. Introduction

HIV/AIDS is a pandemic infection with socio-economic factors associated with HAART non-adherence [1].

It is well established that the clinical efficiency of HAART in suppressing the HIV virus toward a long survival needs a non-adherence rate of less than 5% [2].

South Africa is facing a high level of HIV/AIDS rate [3], where a low level of non-adherence (correct dosage, taken on time and in the correct way, economic/sanitation/food security and safety) is needed [4].

However, it is also known significantly that the perfect non-adherence level should be $\leq 5\%$ to minimize drug resistance and limit AIDS complications [5].

Indeed, the poor HAART adherence rate, less than 95% of prescribed medication (otherwise $\geq 5\%$ non-adherence), is not yet been explored among HIV/AIDS patients attending Lerato clinic in Germiston, South Africa.

This gap motivated the initiation of the present study with the objective to describe the socio-economic factors associated with non-adherence to HAART among patients in the Lerato clinic.

2. Materials and Methods

2.1. Study Design

It was a cross-sectional conducted from September 2019 to December 2019.

2.2. Study Setting

Lerato clinic is an HIV clinic in Bertha Qxowa Hospital located in Germiston, Johannesburg, South Africa, and was selected as our study setting.

2.3. Study Population

All adult HIV-infected patients, on HAART for at least three months and attending during the same period and the setting management of this study.

2.3.1. Sampling

The sample size calculation used the Raosoft software: about 150 patients are seen daily Monday to Friday. Of the patients seen daily approximately, 50 are on HAART. Over the study period, it is estimated that we need approximately 278 participants. This assumes a margin of error of 5%, a confidence level of 95%, and a response distribution of 50%.

Patients were investigated for factors that are associated with their drug non-adherence based on observing the timing of doses and keeping clinic appointments for drug refills during the period of the study.

These patients meeting the criteria for inclusion in the study were invited to participate, examining potential barriers to adherence. The investigator did approach every patient during each daily interview period.

2.3.2. Inclusion Criteria

Those being more than 18-year-old, on HAART for at

least three months, consenting to participate, and attending the clinic were included.

2.3.3. Exclusion Criteria

Patients less than 18-year-old, not speaking English, Tswana, or Zulu, those who are not literate, who cannot communicate in the above-selected languages, and patients on HAART with less than three months of treatment were excluded.

2.4. Data Collection

A precoded and standardized questionnaire was used for data collection. It contains five items that briefly ask for demographic (Gender: male/female, Age: ≥ 45 years/ < 45 years, Ethnic group: Black/White/Coloured/Indian, Marital status: Single/Married/Living with life-partner/Widowed/Separated/Divorced, Level of education: Primary/High school/College/University, and status of employment: Full-time/Sessional/None) information and then poses six closed-ended and a single open-ended question about potential barriers to HAART adherence that patient might identify.

That questionnaire was adapted from the one which has been used in the Botswana study [6].

Data were not collected on Tuesdays as the day is consecrated for academic meetings. All surveys were confidential and anonymous. They were conducted in private by the principal investigator in a separate room in the clinic, where participants were filling in the questionnaire for 45 minutes. Data were collected from the consenting respondents using self-administered questionnaires with the help of an assistant for language barriers, especially for those who cannot communicate in selected languages. The key variables to examine were demographics.

The investigator used a validated questionnaire modeled after the Adult AIDS Clinical Trial Group adherence instrument that was carried out to identify missed doses over a 1-year interval. The investigator did first a pill count for all eligible patients every working day. After answering the questionnaire, the investigator collected it for analysis. The information was drawn from files and the questionnaire. The result was transferred into a data sheet.

2.5. Data Analysis

The files were retrieved from the records department with the help of a clerk working in that department. The information retrieved was recorded on to excel spreadsheet. In an attempt to minimize recall bias, the investigator did ask patients to indicate their non-adherence over the previous day, previous week, previous month, and previous year successively. Non-adherence was defined as taking their medication $\leq 95\%$ of the time. If one is taking a once-daily treatment, it means missing no more than one dose per month, if it's a twice-daily treatment it means missing no more than three doses per month and if one is taking three times a day treatment it means missing no more than four doses per month.

The investigator determined the percentage of patients surveyed and met the criteria for non-adherence.

The analysis was done as follows:

- 1) Determining the percentage of non-adherent participants, as it was found in the sample.
- 2) Demographic data were summarized in a table format.
- 3) Descriptive statistics to describe common factors associated with HAART non-adherence.

Statistical tests were performed to compare the characteristics of adherents and non-adherents. Quantitative variables were converted into qualitative variables that were analyzed using the chi-square test. Logistic regression was used to estimate Odds-Ratios and their confidence interval in univariate and multivariate analyzes. SPSS version 23.1 software was used for all statistical analyzes. Adjusted Odds ratio (aj.OR) and Confidence Interval (CI) 95% were obtained to state significant associations. The criteria for 2-sided statistical significance were defined by a P-value <0.05.

2.6. Ethical Approval and Consent to Participate

The study protocol was approved by the National Human Research Ethics Committee, Kinshasa, D. R. Congo, according to the Declaration of Helsinki III recommendations (Helsinki-Declaration-1964-2015-08-20), and also approved by Betha Qxowa hospital to start the research. The researcher took into consideration the fundamental principles of ethical research.

Written informed consent was obtained from patients for participating. The investigator clearly explained to the study participants what was expected from them and what to do if they decided not to proceed with the study. Whether to participate or not from the very beginning was the decision of the study participants, and they were assured that their refusal to participate in the study would have no consequences. They were also told that they had the right to ask questions at any time and withdraw from the study under any circumstances.

Confidentiality and anonymity for participants were guaranteed as well. The completed questionnaires were kept in a locked drawer in the office of the principal investigator. Data treated were stored in a digital file of which access was only possible through the use of the investigator's password.

3. Results

Out of 278 patients (56%, n= 156 Males; 44%, n= 122 Females) with a sex ratio of 1.3 Male ÷ 1 Female, all were evaluated.

The majority of patients were younger than 45 years (67%, n = 187), single (43%, n = 120), Blacks (75.8%, n = 211), those with High School level (48%, n = 134), and Jobless people (45%, n = 126).

Out of all patients, 19% (n = 52) were recognized as non-adherents to HAART in Lerato clinic in Betha Qxowa Hospital, Germiston, Gauteng, South Africa.

Table 1. Description of socio-demographic parameters.

Parameters	Frequency	Percentage
Gender		
Male	156	56
Female	122	44
Age Categories		
≥45	91	33
<45	187	67
Marital Status		
Single	120	43
Married	47	17
Living with Partner	51	18
Divorced	15	5
Widowed	24	9
Separated	21	8
Ethnic Group		
Black	211	75.8
White	36	12.9
Coloured	13	4.6
Indian	18	6.4
Level of Education		
University	24	9
College	89	32
High School	134	48
Primary	31	11
Employment Status		
Full Time	50	18
Sessional	102	37
None	126	45

Compared to patients with adherence to HAART (Age 45.8 ± 17.7 years)), non-adherent patients to HAART were significantly ($p < 0.005$) younger (Age = 40.3 ± 11.4 years).

Table 2. Non-Adherence to HAART and Socio-demographic Parameters.

Socio-demographic Parameters	Adherence to ARV Treatment		
	Non-adherent	Adherent	P-value
Age (years)			
<45	26 (13.9)	161 (86.1)	0.003
≥45	26 (28.6)	65 (71.4)	
Gender			
Male	37 (23.7)	119 (76.3)	0.011
Female	15 (12.3)	107 (87.7)	
Marital Status			
Single	24 (20.0)	96 (80.0)	0.022
Married	6 (12.8)	41 (87.2)	
Living with Partner	5 (9.8)	46 (90.2)	
Divorced	4 (26.7)	11 (73)	
Widowed	10 (41.7)	14 (58.3)	
Separated	3 (14.3)	18 (85.7)	
Ethnic group			
Black	41 (19.4)	170 (80.6)	0.452
White	5 (13.9)	31 (86.1)	
Coloured	1 (7.7)	12 (92.3)	
Indian	5 (27.8)	13 (72.2)	
Level of education			
University	3 (12.5)	21 (87.5)	0.001
College	5 (5.6)	84 (94.4)	
High School	36 (26.9)	98 (73)	
Primary	8 (25.8)	23 (74)	
Employment status			
Full time	1 (2.0)	49 (98.0)	0.001
Sessional	13 (12.7)	89 (87.3)	
None	38 (30)	87 (69.6)	

There were univariate and significant associations between

male gender, aging ≥ 45 years, Widowed, non-employment, and non-adherence to HAART (Table 2).

However, there was no significant univariate association ($P = 0.452$) between Ethnic groups and non-adherence to HAART: 19.4% ($n = 41/211$) among blacks, 13.9% ($n = 5/36$)

among Caucasians/ Whites, 7.7% ($n = 1/13$) among coloured, and 27.8% ($n = 5/18$) among Indians.

The univariate risk of non-adherence to HAART was respectively multiplied by 2, 3, 5, and 4 by male gender, aging, low education level, and Widowed. (Table 3).

Table 3. Univariate risk factors of non-adherence to HAART.

Univariate risk factors	Non-adherence to HAART% (n)	OR (95% CI)	P-value
Gender			
Males	23.7 (37/156)	2.2 (1.2 – 4.3)	0.015
Females	12.3 (15/122)	1	
Age groups			
≥ 45 years	28.6 (26/91)	2.5 (1.3 – 4.6)	0.003
< 45 years	13.9 (26/187)	1	
Education levels			
Lower/Primary-High School	26.7 (44/165)	4.8 (2.2 – 10.6)	< 0.0001
Higher/College-University	7.1 (8/113)	1	
Married/Widowed			
Yes	41.7 (10/24)	3.6 (1.5 – 8.7)	0.003
No	16.5 (42/254)	1	

After 3 iterations/steps of multivariate binary logistic regression, and excluding confounding variables such as marital status, education levels, only male gender, none

employment, sessional employee, and aging were identified as the most important significant and independent determinants of non-adherence to HAART. (Table 4).

Table 4. Independent determinants of non-adherence to HAART.

Independent variables	B	SE	Wald	df	Adj.OR (95% CI)	P-value
Gender						
Males	0.708	0.353	4.027	1	2 (1.02 – 4.1)	0.045
Females					1	
Employment						
None	3.075	1.034	8.838	1	21.7 (2.9 – 164)	< 0.0001
Sessional				1		
Full-time	2.036	1.059	3.698	1	7.7 (1 – 61.1)	0.05
Age groups						
≥ 45 years	0.909	0.333	7.447	1	2.5 (1.3 – 4.8)	0.006
< 45 years				1		
Constant	-4.723	1.060	19.837	1		< 0.0001

4. Discussion

The present study, carried out in South Africa among a multi-ethnic community, sought to demonstrate significant associations between some socio-economic factors and non-adherence to HAART as highlighted by different publications in the literature [1-5].

The burden of non-adherence to HAART was estimated at 19% within this study, which is lower than what was observed in neighboring countries, Kenya [7], and Sudan [8], where the non-adherence rate was more than 20%. This non-adherence rate was also near to the other studies conducted in different regions of Ethiopia, Addis Ababa [9], Debreziet [10], and Jimma [11]. The low-level non-adherence helps to control and suppress the viral load [12]. It is found that most African countries achieved an excellent rate of non-adherence when compared to their North-American counterparts estimated at 23%; this may be due to the availability of subsidized ART medication [13, 14].

The possibility of lower non-adherence might be due to (a) self-reported non-adherence, (b) limited to the first-line

regimen, and (c) exclusion of patients who were not interested.

Also, many factors associated were consistent with other studies from developing and developed countries. In our study, the males' ratio showed the highest non-adherence than females, this finding was not in line with other studies like in Ethiopia [15]. Since males are busy drinking alcohol and other drugs, the chances of forgetting their doses were high. The reported reasons for non-adherence in African studies include forgetting, travel, fear of disclosure, shortage of pills, difficult schedules, cost, lack of access, and privacy [16].

In a cohort study of ARV adherence among semi-urban South African living in extreme poverty, Byakika-Tusiime et al. found that lower socioeconomic status was not a predictor of non-adherence for patients with fully subsidized therapy [17]. In fact, non-adherence levels were similar to or better than those found in industrialized countries. Similarly, low levels of non-adherence (22%) were reported by Laurent et al [18]. In a resource-poor setting in Senegal and 34% in 3 treatment centers in Kampala, Uganda, non-adherence in our study was higher

than the levels reported by Orrell *et al.* [19] but lower than that reported by Laurent *et al.* and Byakika-Tusiime *et al.* leave our non-adherence rate within the range of non-adherence rates of people living with HIV/AIDS (PLWHA) to HAART in African settings. The most reasons for missing doses were being away from home, forgetting, and being too busy. The most important factors associated with decreased non-adherence include the educational level of the patient.

Contrarily to the Nigerian study [20] where marital status was not significant for non-adherence, our study found that being alone (single, separated, divorced, and widowed) was associated with non-adherence to HAART. Maybe loneliness, depression, and low income might explain poor adherence to HAART in this study.

Indeed, marital disruption has a relationship with major depression [21], which is related to non-adherence to HAART.

Apartheid, the Afrikaans name was given by white-ruled South Africa's Nationalist Party in 1948. This might explain the lack of significant association between ethnicity/racism and non-adherence to HAART in this study conducted in a democratic republic of South Africa [22].

It was also found in the study done that not receiving practical social support was associated with a higher rate of non-adherence as a single predictor [23].

5. Conclusion

Our study found the level of non-adherence to be 19%, very high, but comparable to other developing countries. Stigma or fear of disclosure, being away from home, too busy with other things, the side-effects, and toxicity of ART drugs, are the main obstacles to ART adherence.

Apartheid and other social behavior played a great role in this non-adherence to HAART.

There is also a need for effective and sustainable information, education, and communication strategy in Lerato clinic to address the problem of HIV stigma and gender discrimination, which is a proven barrier to care and adherence to therapy. Government and non-governmental agencies are particularly joined to make this a priority for lasting HIV/AIDS prevention and control in the Lerato clinic, Gauteng, South Africa.

Expanded access to subsidized ART should improve adherence and, consequently, treatment outcomes for patients receiving therapy in resource-poor settings.

Conflicts of Interest

The authors declare that they have no competing interests.

Acknowledgements

We would like to thank Lomo University of Research (LUR), Bertha Qxowa Hospital, and Lerato clinic for allowing us to do this study.

References

- [1] Plymoth M., Sanders E. J., Van Der Elst E. M., Medstrand P., Tesfaye F., Winqvist N., Balcha T., Björkman P. Socio-economic condition and lack of virological suppression among adults and adolescents receiving antiretroviral therapy in Ethiopia. Available at <https://doi.org/10.1371/journal.pone.0244066>. (Accessed: 1 April 2022).
- [2] HIV/AIDS. Available at <https://epicentre.msf.org/en/our-achievements/hivaids>. (Accessed: 1 April 2022).
- [3] Allinder SM and Fleischman J. The World's Largest HIV Epidemic in Crisis: HIV in South Africa. Center for strategic and international studies 2019, April. Available at <https://www.csis.org/analysis/worlds-largest-hiv-epidemic-crisis-hiv-south-africa>. (Accessed: 25 April 2022).
- [4] Peltzer K, Pengpid S. Socioeconomic factors in adherence to HIV therapy in low- and middle-income countries. *J Health Popul Nutr.* 2013 Jun; 31 (2): 150-70. doi: 10.3329/jhpn.v31i2.16379. PMID: 23930333; PMCID: PMC3702336.
- [5] Jacob S A *et al.* "Improving the Adherence to Antiretroviral Therapy, a Difficult but Essential Task for a Successful HIV Treatment-Clinical Points of View and Practical Considerations." *Frontiers in pharmacology* vol. 8 831. 23 Nov. 2017, doi: 10.3389/fphar.2017.00831.
- [6] Kip E, Ehlers VJ and Van der Wal DM. (2009). Patients' Adherence to Anti-Retroviral Therapy in Botswana. *Journal of Nursing Scholarship* 41 (2): 149-57. Available at https://www.researchgate.net/publication/26303547_Patients'_Adherence_to_Anti-Retroviral_Therapy_in_Botswana. (Accessed: 23 January 2022).
- [7] Mukui IN, Ng'ang'a L, Williamson J, Wamicwe JN, Vakil S, Katana A, *et al.* Rates and predictors of non-adherence to antiretroviral therapy among HIV-positive individuals in Kenya: Results from the second Kenya AIDS indicator survey, 2012. *PLoS One* 2016; 11: e0167465.
- [8] Ibrahim Y, Sutan R, Latif KA, Al-Abed AA, Amara A, Adam I. Poor adherence to antiretroviral therapy and associated factors among people living with HIV in Omdurman city, Sudan. *Malays J Public Health Med* 2014; 14: 90-101.
- [9] Tadios Y, Davey G. Antiretroviral treatment adherence and its correlate in Addis Ababa, Ethiopia. *Ethiop Med J* 2006; 44: 237-44.
- [10] Ayalew M. Assessment of Adherence to Antiretroviral Therapy Among Hiv-Infected Persons in the Ministry of National Defense Force Hospitals, Addis Ababa And Debreziet. (Doctoral Dissertation, Aau); 2005.
- [11] Miftah A. Antiretroviral Treatment Adherence and Its Determinants among People Living With HIV/AIDS on Highly Active Antiretroviral Therapy at Two Hospitals in Oromiya Regional State, Ethiopia. (Doctoral Dissertation, Aau); 2006.
- [12] Rosenblum M, Deeks SG, van der Laan M, Bangsberg DR. The risk of virologic failure decreases with duration of HIV suppression, at greater than 50% adherence to antiretroviral therapy. *PLoS One* 2009; 4: e7196.

- [13] Byakika-Tusiime J, Oyugi JH, Tumwikirize WA, Katabira ET, Mugenyi PN, Bangsberg D. Ability to purchase and secure stable therapy are significant predictors of non-adherence to antiretroviral therapy in Kampala, Uganda. In: Tenth Conference on Retroviruses and Opportunistic Infections. Boston, USA; 2003.
- [14] Laurent C, Fatou N, Gueye NF, Diakhaté N, Ndir A, Gueye M, et al. Long-term follow-up of a cohort of patients under HAART in Senegal. In: 10th Conference on Retroviruses and Opportunistic Infections. Boston, MA, USA; 2003. p. 10-4.
- [15] Jima F, Tatiparthi R. Prevalence of nonadherence and its associated factors affecting on HIV adult's follow-up at an antiretroviral therapy clinic in Batu Hospital, Eastern Ethiopia. *Indian J Sex Transm Dis* 2018; 39: 91-7.
- [16] Day J, Godoka N, Nyamafeni P, Chigwanda M. Adherence to ART in clinical trial settings in Zimbabwe and Uganda: Lessons learned. In: Proceedings of the International AIDS Conference; 2002.
- [17] Byakika-Tusiime J, Polley EC, Oyugi JH, Bangsberg DR. Free HIV antiretroviral therapy enhances adherence among individuals on stable treatment: implications for potential shortfalls in free antiretroviral therapy. *PloS one* 2013; 8: e70375.
- [18] Laurent C, Diakhate N, Gueye NF, Touré MA, Sow PS, Faye MA, Gueye M, Lanièce I, Kane CT, Liégeois F, Vergne L. The Senegalese government's highly active antiretroviral therapy initiative: an 18-month follow-up study. *Aids* 2002; 16: 1363-70.
- [19] Orrell C, Cohen K, Mauff K, Bangsberg DR, Maartens G, Wood R. A randomized controlled trial of real-time electronic adherence monitoring with text message dosing reminders in people starting first-line antiretroviral therapy. *JAIDS* 2015; 70: 495-502.
- [20] Ijeoma Okoronkwo, Uchenna Okeke, Anthonia Chinweuba, Peace Iheanacho, "Nonadherence Factors and Sociodemographic Characteristics of HIV-Infected Adults Receiving Antiretroviral Therapy in Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria", *International Scholarly Research Notices*, vol. 2013, Article ID 843794, 8 pages, 2013. <https://doi.org/10.1155/2013/843794>
- [21] Bulloch AG, Williams JV, Lavorato DH, Patten SB. The relationship between major depression and marital disruption is bidirectional. *Depress Anxiety*. 2009; 26 (12): 1172-7. doi: 10.1002/da.20618. PMID: 19798680.
- [22] The end of Apartheid. Archives of the US Department of State. Available at <https://2001-2009.state.gov/r/pa/ho/time/pcw/98678.htm>. (Accessed: 26 April 2022).
- [23] Zwikker HE, van den Bemt BJ, Vriesevink JE, van den Ende CH, van Dulmen S. Psychosocial predictors of non-adherence to chronic medication: systematic review of longitudinal studies. *Patient Prefer Adherence*. 2014; 8: 519-563. Published 2014 Apr 25. doi: 10.2147/PPA.S47290.